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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,645	07/23/2003	Claudio Pisano	4865-74	6903

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
03/27/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/624,645	PISANO ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71-106* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-30-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The RCE dated 10-30-07 is acknowledged.

Claims included in the prosecution are 71-106.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 79-93 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A cosmetic by definition is meant for the external organs such as skin. It is unclear as to why a cosmetic is delivered intracellularly. If it is delivered intracellularly and has a function, then it is a therapeutic agent.

This rejection is maintained since applicant has not addressed this issue.

According to claim 86, the composition is a liposome composition containing camptothecin; the last line of the claim however, recites, "said liposome comprising a substance with cosmetic activity". Camptothecin is an anti-cancer agent and not a cosmetic agent. Furthermore, if the compound is a cosmetic agent, then claim 93 which recites various modes of administration is inconsistent with a cosmetic substance since a cosmetic substance is administered only topically.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 71-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al in combination with Allen (6,056,973), Burke (5,552,156), in further combination with Stracher (5,008,288).

Wang et al disclose cationic liposome compositions containing claimed alky acyl carnitine esters for gene delivery. The fatty acid groups are oleyl or myristoyl, palmitoyl or stearoyl groups. The liposomes contain helper lipid (DOPC), cholesterol. The liposomes are administered intravenously (abstract, Scheme 1 on page 2208, Tables 3 and 4 on page 2211, page 2214, col. 2).

What is lacking in Wang et al is the teaching of the use of claimed drugs such as anti-cancer drugs, camptothecins in particular.

Allen teaches that liposomes are delivery agents for anticancer drugs such as camptothecin derivatives and genes (abstract, col. 16, lines 10-17).

Burke teaches that liposome stabilize camptothecin derivatives (abstract, examples and claims).

Stracher teaches that because of the presence of carnitine or its derivatives as

part of liposomal structure, the drug containing liposomes will be delivered in much greater amounts to the desired target organs and much less is metabolized by the liver (abstract, col. 17, line 51 through col. 18, line 44).

It would have been obvious to one of ordinary skill in the art to use the liposomes of Wang et al to delver drugs other than genes, such as anti-cancer drugs or cosmetic agents with a reasonable expectation of success since liposomes are known drug and cosmetic agent carriers and as evident from Allen, the term drug encompasses genes and anti-cancer agents such as camptothecin derivatives and liposomes are carriers for both genes and anti-cancer agents. One of ordinary skill in the art would use camptothecin derivatives as drugs since they are known to be encapsulated in liposomes because of stabilization by liposomes as taught by Burke. One of ordinary skill in the art would be motivated to use carnitine derivatives containing liposomes of Wang et al for the delivery of camptothecin derivatives of Burk since Stracher teaches the advantages of the presence of carnitine derivatives in liposomal structure in the drug delivery.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that there are two sets of claims, method and the composition and that the office action made no distinction between to these. The examiner points out that the method claims are directed to intracellular delivery of the composition and the references teach intracellular delivery. Wang in particular teaches that the composition is for the delivery of genes, which implies that the genes are delivered inside the cells for their function. Applicant argues that the documents are illogically combined to

construct the two prior art-based rejections given in items 4 and 5 of the office action in that the combination of documents does not arrive at the claimed subject matter and in fact certain combinations would not produce a viable product/workable result. According to applicant, Wang et al solve the problem of DNA delivery in gene therapy by providing a liposome made of a number of L-carnitine which efficiently complex with DNA and that no suggestion is given in Wang to use this liposomes to deliver drugs. The examiner points out that if Wang has suggested the drug delivery, the reference in itself would have been a 103 reference. The claimed drugs however, are disclosed by the secondary references and Allen in fact teaches that either genes or camptothecin derivatives can be delivered by liposomes. Applicant argues that Allen discloses liposome composition comprising a liposome made of cationic lipids and does not disclose esters of L-carnitine made liposomes, which entrap taxol or camptothecin. This argument is not persuasive since Allen is combined for its teachings of the use of liposomes for the delivery of both genes and camptothecins. Therefore, it would have been obvious to one of ordinary skill in the art to use Wang's liposomes for the delivery of even camptothecin since Allen teaches the use of liposomes for the delivery of either of these agents.

Applicant argues that Burke overcomes the problems of insolubility and instability of camptothecin drugs administered in their free from by providing that the lactone of the camptothecin drugs administered in their free form by providing that the lactone of the camptothecin structure is intercalated in the bilayer of the liposome so that the ring is protected from hydrolysis and that the liposomes are phospholipids and not carnitine.

This argument is not persuasive. First of all, instant claim language does not exclude phospholipids. Secondly, since camptothecin being hydrophobic, one would expect its incorporation into the liposomal bilayer and obtain similar stability since Wang's liposomes contain even a phospholipid. Applicant argues that in Stracher L-carnitine is only taught to be selective carrier for a drug specific to cardiac and skeletal muscle and no indication is given that an ester of an alkanoyl L-carnitine can be employed to prepare a cationic liposome for selective delivery to target organs for antitumor drugs such as camptothecin and taxol. This argument is not persuasive since instant claims do not exclude cardiac and skeletal muscles and applicant has not shown any unexpected results by using a carnitine derivative instead of carnitine or other carnitine derivatives taught by Stracher.

5. Claims 79-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hsu (5,653,996) in combination with Wang et al cited above.

Hsu discloses liposomal compositions for the delivery of therapeutic or cosmetic agents. The agents include plasmids (DNA), a variety of passenger molecules. The compositions can be administered topically (col. 4, lines 53-55, col. 6, line 10 through col. 8, line 1, col. 14, lines 52-56, col. 15, lines 1-9).

What is lacking in Hsu is the teaching of the inclusion of claimed carnitine derivatives.

Wang as discussed above teaches the ability of the claimed carnitine derivatives to form liposomes by themselves or in combination with other bilayer forming phospholipids (abstract).

It would have been obvious to one of ordinary skill in the art to use the liposomes of Wang in the teachings of Hsu for the delivery of therapeutic as well as cosmetic agents with a reasonable expectation of success since both Wang and Hsu are directed to liposomes and liposomes are carriers of active agents.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments regarding Wang have already been addressed by the examiner. Applicant argues that Hsu is a general disclosure relating to liposomes, which can be made by phospholipids and others for the delivery of active agents, and Hsu does not specifically disclose a carnitine/acyl L-carnitine made liposomes for selective delivery of taxol or camptothecin. This argument is not persuasive. First of all, instant claims recite cosmetic agent and Hsu teaches cosmetic agents. Hsu also teaches genes and other therapeutic agents. Hsu in particular teaches on col. 7, lines 41-42 teaches tumoricidal agents, though not specifically taxol and camptothecins. Applicant has not shown any unexpected results obtained by using the claimed tumoricidal agents namely taxol and camptothecins.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612

GSK